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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/800,541	03/07/2001	Liselotte Bjerre Knudsen	6169.200-US	4130

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NOVO NORDISK, INC.
PATENT DEPARTMENT
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EXAMINER	
ROMEO, DAVID S	
ART UNIT	PAPER NUMBER
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/800,541	KNUDSEN, LISELOTTE BJERRE	
	Examiner	Art Unit	
	David S. Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26,28,29,36,43-50 and 73-80* is/are pending in the application.

4a) Of the above claim(s) *44 and 45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26,28,29,36,43,46-50 and 73-80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *26,28,29,36,43-50 and 73-80* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

The amendment filed 12/22/2006 has been entered. Claims 26, 28, 29, 36, 43–50 and 73–80 are pending. Applicant's elected group I, claims 26–29 and 36–42, and the species Arg^{34},Lys^{26}(N^{ε}-(γ-Glu(N^{α}-hexadecanoyl)))GLP-1(7-37) in the paper filed 11/08/2002. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 26, 28, 29, 36, 43–50 and 73–80 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) to the extent that they are drawn to a nonelected species, there being no allowable generic or linking claim. Claims 44–45 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/08/2002.

Claims 26, 28, 29, 36, 43, 46–50 and 73–80 are being examined to the extent that are directed to the elected species Arg^{34},Lys^{26}(N^{ε}-(γ-Glu(N^{α}-hexadecanoyl)))GLP-1(7-37) and GLP-1 (7-36)amide.

Maintained Formal Matters, Objections, and/or Rejections:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 26, 28, 29, 36, 46–50 and 73–80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beeley (WO 98/30231) in view of Knudsen (WO 98/08871).

Applicants argue that Knudsen cannot cure the deficiencies of Beeley; that Beeley relates to the use of exendin-3 or exendin-4, neither of which are recited in the present claims; that Knudsen merely relates to known GLP-1 analogues; that thus, the combination of these three references doesn't get one to the presently claimed method for lowering levels of triglycerides and/or free fatty acids by administering to a patient a GLP-1 agonist, as defined herein, wherein the treated patient is not receiving insulin treatment.

Applicants' arguments have been fully considered but they are not persuasive. The rejection was originally made in the alternative as obvious over Beeley or Juntti-Berggren in view of Knudsen (WO 98/08871). Applicants amendment has overcome Juntti-Berggren in view of Knudsen. However, the rejection under 35 U.S.C. 103(a) as being unpatentable over Beeley (WO 98/30231) in view of Knudsen (WO 98/08871) is maintained.

Beeley teaches a method for lowering plasma lipids or reducing cardiac risk comprising administering to a subject afflicted with obesity and type 2 diabetes a therapeutically effective amount of an exendin or an exendin agonist, as indicated in the last Office action. Insofar as Beeley does not require treatment or co-treatment with insulin, then Beeley's treatment method is directed a patient "not receiving insulin treatment."

Beeley also discloses that exendins bind GLP-1 receptors (page 4, lines 20-24). Therefore, exendins are GLP-1 agonist. It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to administer an exendin or exendin agonist, as taught by Beeley, and to modify that teaching by administering Arg^{34},Lys^{26}(N^{ε}-(γ-Glu(N^{α}-

hexadecanoyl)))GLP-1(7-37), as taught by Knudsen, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification because Arg^{34},Lys^{26}(N^{ε}-(γ-Glu(N^{α}-hexadecanoyl)))GLP-1(7-37) is a GLP-1 agonist that has a more protracted profile of action.

The lowering of triglycerides and free fatty acids is an additional advantage associated with doing what the prior art suggests and does not lend patentability to an otherwise unpatentable invention. The lowering of triglycerides and free fatty acids would flow naturally from following the suggestion of Beeley in view of Knudsen.

The invention is prima facie obvious over the prior art.

Double Patenting

Claims 26, 28, 29, 36, 46–50 and 73–80 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 39, 40 of U.S. Patent No. 6,268,343 in view of Beeley (WO 98/30231).

Applicants argue that the obviousness-type double patenting rejection over claims 39-40 of US 6,268,343 (US 343) in view of Beeley has been obviated by appropriate amendment; that claims 39-40 of US '343 recite a method of treating diabetes or obesity, respectively, comprising administering a GLP-I derivative of claim 1; that US '343 is completely silent regarding a method of lowering serum levels of triglycerides and/or free fatty acids; that Beeley relates to exendins, US '343 does not; that another problem is that Juntti-Berggren relates to dual therapy with insulin and GLP-1 (7-36) amide, which is not part of the present claims, and Juntti-Berggren repotted that this treatment had no effect on the levels of LDL and HDL cholesterol;

that there would be no reason to think that the derivatives of US '343 would be useful in lowering triglycerides or free fatty acids in view of the effects of exendins described in Beeley.

Applicants' arguments have been fully considered but they are not persuasive. Although the patent's claims are silent with respect to lowering lipid levels, Beeley teaches a method for lowering plasma lipids or reducing cardiac risk comprising administering to a subject afflicted with obesity and type 2 diabetes a therapeutically effective amount of an exendin or an exendin agonist. Beeley also discloses that exendins bind GLP-1 receptors (page 4, lines 20-24). Therefore, exendins are GLP-1 agonist. It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention that a method of treating obesity or diabetes with a GLP-1 analog, such as the GLP-1 analog Arg^{34},Lys^{26}(N^{ε}-(γ-Glu(N^{α}-hexadecanoyl)))GLP-1(7-37) taught in the patent's claims, is a method of lowering plasma lipid levels. The lowering of triglycerides and free fatty acids is an additional advantage associated with doing what the patent in view of Beeley suggests and does not lend patentability to an otherwise unpatentable invention. The lowering of triglycerides and free fatty acids would flow naturally from following the teachings of the patent's claims.

Claims 26, 28, 29, 36, 46–50 and 73–80 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 19, 20 of U. S. Patent No. 6,458,924 in view of Beeley (WO 98/30231).

Applicants argue that the obviousness-type double patenting rejection of claims 26-29, 36-42, 44-50, 52, 54-60, 62, 64-70, 72-73, and 76 (now 26, 28-29, 36, 44-50, 73, and 76) over claims 19-20 US 6,458,924 (US '924) in view of Beeley has been obviated by appropriate

amendment. Claims 19-20 of US '924 recite a method of treating diabetes or obesity, respectively, comprising administering a GLP-I derivative of claim 1. US '924 is completely silent regarding a method of lowering serum levels of triglycerides and free fatty acids. The Office Action states that since Beeley cures the deficiency of US '924 by describing a method of lowering plasma lipids etc. by administering an exendin agonist. The problem is, Beeley relates to exendins, US '924 does not. Another problem is that Juntti-Berggren relates to dual therapy of insulin and GLP-1 (7-36) amide, which is not part of the present claims, and Juntti- Berggren reported that this treatment had no effect on the levels of LDL and HDL cholesterol. In light of the above, there would be no reason to think that the derivatives of US '924 would be useful in lowering triglycerides or free fatty acids in view of the effects of exendins described in Beeley. Withdrawal of this rejection is respectfully requested.

Applicants' arguments have been fully considered but they are not persuasive. Although the patent's claims are silent with respect to lowering lipid levels, Beeley teaches a method for lowering plasma lipids or reducing cardiac risk comprising administering to a subject afflicted with obesity and type 2 diabetes a therapeutically effective amount of an exendin or an exendin agonist. Beeley also discloses that exendins bind GLP-1 receptors (page 4, lines 20-24). Therefore, exendins are GLP-1 agonist. It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention that a method of treating obesity or diabetes with a GLP-1 analog, such as the GLP-1 analog Arg^{34},Lys^{26}(N^{ε}-(γ-Glu(N^{α}-hexadecanoyl)))GLP-1(7-37) taught in the patent's claims, is a method of lowering plasma lipid levels. The lowering of triglycerides and free fatty acids is an additional advantage associated with doing what the patent in view of Beeley suggests and does not lend patentability to an otherwise unpatentable

invention. The lowering of triglycerides and free fatty acids would flow naturally from following the teachings of the patent's claims.

New Formal Matters, Objections, and/or Rejections:

Formal Matters

The application is not fully in compliance with the sequence rules, 37 C.F.R. § 1.821-1.825. Specifically, the claim 26 fails to recite the appropriate sequence identifiers at each place where a sequence is discussed. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. The application cannot issue until it is in compliance. Nucleic acid sequences with 10 or more nucleotides, at least 4 of which are specifically defined, must comply with the sequence rules. Amino acid sequences with 4 or more residues, at least 4 of which are specifically defined, must comply with the sequence rules. Sequence identifiers can also be used to discuss and/or claim parts or fragments of a properly presented sequence. For example, language such as "residues 14 to 243 of SEQ ID NO: 23" is permissible and the fragment need not be separately presented in the "Sequence Listing."

Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 73–76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 73–76 are indefinite because they depend, either directly or indirectly, from a canceled claim, and thus makes no sense, since they are incomplete. The metes and bounds are not clearly set forth. In the interest of compact prosecution the claim will be interpreted as incorporating the limitations of claim 26. However, this interpretation of the claim does not relieve applicant from the requirement to respond to the instant rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 26, 29, 36, 43, 73, 76, 77 and 80 are rejected under 35 U.S.C. 102(b) as being anticipated by Efendic (U. S. Patent No. 5,631,224) as evidenced by Kreisberg (Am J Cardiol. 1998 Dec 17;82(12A):67U-73U).

Efendic discloses the treatment of type 2 diabetes with GLP-1(7-36) amide (column 4, lines 47-50). Insofar as Efendic does not require treatment with insulin, then Efendic discloses the treatment of patients having type 2 diabetes wherein the patients are not receiving insulin treatment. Type-2 diabetic patients are in need of having triglycerides and free fatty acids lowered as evidenced by Kreisberg. Specifically, Kreisberg discloses that lipoprotein abnormalities are manifested during the largely asymptomatic diabetic prodrome and contribute substantially to the increased risk of macrovascular disease. The insulin-resistant diabetes course affects virtually all lipids and lipoproteins. See the Abstract, page 67U.

A chemical composition and its properties are inseparable. Therefore, Efendic's GLP-1(7-36) amide lower triglycerides and free fatty acids.

Information Disclosure Statement

In the Office action mailed 12/02/2003 the examiner inadvertently omitted his initials next to the Young reference on the Information Disclosure Statement filed 10/14/2003. A copy of the Information Disclosure Statement filed 10/14/2003 is included in the present Office action, indicating that the Young reference has been considered.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 9:00 A.M. TO 5:30 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571) 272-0961.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-8300.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING MAY BE OBTAINED FROM THE PATENT APPLICATION INFORMATION RETRIEVAL (PAIR) SYSTEM. STATUS INFORMATION FOR PUBLISHED APPLICATIONS MAY BE OBTAINED FROM EITHER PRIVATE PAIR OR PUBLIC PAIR. STATUS INFORMATION FOR UNPUBLISHED APPLICATIONS IS AVAILABLE THROUGH PRIVATE PAIR ONLY. FOR MORE INFORMATION ABOUT THE PAIR SYSTEM, SEE HTTP://PAIR-DIRECT.USPTO.GOV. CONTACT THE ELECTRONIC BUSINESS CENTER (EBC) AT 866-217-9197 (TOLL-FREE) FOR QUESTIONS ON ACCESS TO THE PRIVATE PAIR SYSTEM,

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
MARCH 19, 2007

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES	Application No. 09/800,541	Applicant(s) KNUDSEN, LISELOTTE BJERRE	
	Examiner David S. Romeo	Art Unit 1647	

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒7. Other: The claims fail to recite the appropriate sequence identifier, i.e., "SEQ ID NO:".

Applicant Must Provide:

☐ computer readable form (CRF) copy of the "Sequence Listing".

☐ paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☐ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (571)272-2510
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